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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
VENCI, DAVID J	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 07/01/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/252,828	DONG ET AL.	
	Examiner	Art Unit	
	David J Venci	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 May 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *69-78* is/are pending in the application.

4a) Of the above claim(s) *73-78* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *69-72* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *03 October 2003 and 18 May 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Examiner acknowledges Applicants' amendment filed 11/19/03, which canceled all pending claims (i.e. claims 48-68) and added new claims 69-78.

Examiner acknowledges Applicants' supplemental amendment filed 5/18/04, which made several amendments to the specification, sequence listing, claims, and drawings.

Currently, claims 69-78 are before the Office.

Election/Restrictions

Newly submitted claims 73-78 are directed to an invention that is independent or distinct from the invention originally claimed.

Claims 73 and 74 are directed to polypeptides and glycopolypeptides comprising materially different amino acid sequences as evidence by separate amino acid position substitutions. These separate polypeptides and glycopolypeptides bear distinct structural or biochemical properties as substantiated by the separate amino acid substitution positions thereby having different binding characteristic and functionality. Therefore, each disclosed patentably distinct glycopolypeptide is considered a separate invention and changes the scope of the previously elected invention.

Claims 75-78 are directed to a human ovarian cell containing a vector.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 73-78 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Specification

The disclosure is objected to because of the following informalities:

The substitute raw sequence listings filed November 14, 2000 and May 18, 2004 are objected to under 35 U.S.C. 132 because they introduce new matter into the disclosure. Under 35 U.S.C. 132, no amendment shall introduce new matter into the disclosure of the invention. The added material that is not supported by the original disclosure can be found under the listing for SEQ ID NO: 3. Specifically, the description of the organism has been changed from "mouse" to "murine sp." Applicant is required to cancel the new matter in the reply to this Office Action.

In addition, Applicants' have amended the specification to include reference to a "Table 1" (p. 15, line 2). See also p. 10, line 13. Currently, there is no such table of record. If applicants wish to add a table to the specification at a later date, applicants must pay careful attention not to add new matter. Clarification is required.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 70 and 72 are directed to non-statutory subject matter. Specifically, claims 70 and 72 read on products of nature. Amendment of these claims to recite "isolated" or "recombinantly produced" polypeptides or glycopolypeptides will obviate this rejection.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 69-72 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chamberlin & Dean, 87 PROC. NATL. ACAD. SCI. 6014 (1990) in view of Kinloch et al., 92 PROC. NATL. ACAD. SCI. USA 263 (1995).

Chamberlin & Dean teach a human ZP3 protein comprising the amino acid sequence of the claimed SEQ ID NO: 2 (See p. 6017, Fig. 3).

Chamberlin & Dean do not teach a recombinantly produced polypeptide. Chamberlin & Dean also do not teach a glycopolypeptide.

However, Kinloch et al. teach a recombinantly produced ZP3 polypeptide and glycoprotein (See p. 264, GLYCOPROTEIN PURIFICATION) in order to create and test mutant ZP3 proteins for sperm-binding activity.

Therefore, it would have been obvious for a person of ordinary skill in the art to combine the ZP3 amino acid sequence of Chamberlin & Dean with the method of making recombinant ZP3 protein of Kinloch et al. in order to produce a recombinant ZP3 polypeptide or glycopolypeptide. Kinloch et al. provide motivation by teaching the importance of a specific portion of ZP3 glycopeptide located in the carboxy-terminal end of both mouse and human ZP3 protein (See p. 267, col. 1, lines 29-51). Kinloch et al. then sets forth a method of producing mouse and chimeric human ZP3 protein (See p. 264, GLYCOPROTEIN PURIFICATION).

Claims 71 and 72 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chamberlin & Dean, 87 PROC. NATL. ACAD. SCI. 6014 (1990) in view of Kinloch et al., 92 PROC. NATL. ACAD. SCI. USA 263 (1995) and Rosiere & Wasserman, 154 DEV. BIOL. 309 (1992).

For a discussion of Chamberlin & Dean and Kinloch et al., see *supra*.

Chamberlin & Dean do not teach a conservatively substituted amino acid sequence of SEQ ID NO:2.

However, Rosiere & Wasserman teach the general location in mouse ZP3 protein sequence responsible for sperm-binding activity (See p. 314, col. 1, lines 31-35). Specifically, Rosiere & Wasserman identify a particular peptide fragment derived from the carboxy-terminal end of the mouse ZP3 protein (See p. 314, col. 2, lines 19-27). It is noted that Applicants' also derived SEQ ID NO: 2 from the carboxy-terminal end of human ZP3 (See specification, p. 6, lines 28-30).

Kinloch et al. extend the knowledge of the art by pointing to the exact amino acid residues of human ZP3 likely responsible for sperm binding (See p. 267, col. 1, lines 29-

51) and describing site-directed ZP3 mutant proteins (See p. 263, col. 2, PLASMID CONSTRUCTION FOR SITE-DIRECTED MUTAGENESIS) in order to map the mouse ZP3 sperm binding site.

Therefore, it would have been obvious to a person of ordinary skill in the art to combine the peptide of Chamberlin & Dean to the ZP3 mutants of Kinloch et al. to provide a peptide of SEQ ID NO: 2 with conservative amino acid substitutions.

Chamberlin & Dean provide motivation by teaching the similarity between mouse and human ZP genes (See p. 6014, col. 2, lines 16-18). According to Chamberlin & Dean, mouse and human ZP3 share 67% identity (See Chamberlin & Dean, p. 6016, col. 2, lines 14-22). Persons of ordinary skill in the art would recognize this as a high degree of homology.

Rosiere & Wasserman extend the knowledge in the art by determining the general location within the mouse ZP3 protein sequence responsible for sperm-binding activity (See p. 314, col. 1, lines 31-35). Specifically, Rosiere & Wasserman identify a particular peptide fragment derived from the carboxy-terminal end of the mouse ZP3 protein (See p. 314, col. 2, lines 19-27). It is noted that Applicants' also derived SEQ ID NO: 2 from the carboxy-terminal end of human ZP3 (See specification, p. 6, lines 28-30). Rosiere & Wasserman teach that this fragment from the carboxy-terminal end of ZP3 is heavily glycosylated and make the following suggestion:

> *"Identification and modification of these* [glycosylation] *sites (e.g., by site-directed mutagenesis or exon swapping) should lead to a better understanding of the molecular basis of carbohydrate-mediated, species-specific gamete interaction in mammals."* (p. 316, col. 1, lines 10-14)

Finally, Kinloch et al. extend the knowledge in the art by pointing to the exact amino acid residues of human ZP3 likely responsible for sperm binding (See p. 267, col. 1, lines 29-51), including Ser342 (lines 41-3). When the amino acid sequence of Kinloch et al. (See Fig. 1) is aligned with the sequence of Chamberlin & Dean (See Fig. 3) and the claimed SEQ ID NO:2, it appears that Ser342 aligns with Ser34 of the claimed SEQ ID NO:2.

As evidenced by Kinloch et al., the concept of creating mutant ZP3 proteins and subsequent testing for sperm-binding activity is a well-known and routine practice in the art. Once Rosiere & Wasserman identified the general region on the ZP3 protein likely to be responsible for sperm-binding activity (i.e. the carboxy-terminal region), a person of ordinary skill in the art would have considered the construction of mutant ZP3 proteins, including a conservative substitution at Ser34 of SEQ ID NO:2 as routine experimentation. By Applicants' admission, the choice of amino acid for substitution (i.e. conservative substitutions) is also known in the art (See specification, p. 11, lines 6-20). Therefore, Applicants' claimed polypeptide having conservative amino acid substitutions is an obvious improvement over the teachings of Chamberlin & Dean, Rosiere & Wasserman, and Kinloch et al.

Claims 71 and 72 recite the claim language "wherein said polypeptide binds human spermatozoa at least ten times as strong as an equivalent molar amount of mouse ZP3." Examiner interprets this recitation as functional language that is not given patentable weight.

Response to Arguments

With respect to prior 112, first paragraph rejections, Applicants' arguments filed 10/03/2003 (See "Section V") have been carefully considered and are persuasive in light of subsequent claim cancellations and amendments. With respect to claims 69-72, the prior 112, first paragraph rejections are withdrawn.

With respect to prior 102(b) and 102(e) rejection based on Dean (US 5,641,487), Applicants' arguments filed 10/03/2003 (See "Section VI") have been carefully considered. The prior 102(b) and 102(e) rejection based on Dean (US 5,641,487) is withdrawn in light of recent amendments to the claims and in light of the rejection presented in the current action based on Chamberlin & Dean, 87 PROC. NATL. ACAD. SCI. 6014 (1990). Applicants assert that Dean does not anticipate new claims 69-78 because Dean does not teach the polypeptide of SEQ ID NO:2. Applicants' arguments have been carefully considered but are not persuasive. Both Dean and Chamberlin & Dean substantially disclose the claimed SEQ ID NO:2. Applicants are claiming a

polypeptide comprising SEQ ID NO:2. The use of open claim language "comprising" allows for anticipation by sequences having additional amino acid residues. "When an examiner obtains a product which reasonably appears to fall within the scope of that which is claimed by a patent applicant, it is reasonable to shift the burden to the applicant to provide evidence showing that the product of the prior art does not fall within the scope of applicants' claims." Ex parte Maizel, 27 USPQ2d 1662, 1667 (BPAI 1992) (citing In re Swinehart, 439 F.2d 210, 169 USPQ 226 (CCPA 1971); In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald, 619 F.2d 67, 205 USPQ 594 (CCPA 1980).

With respect to prior 103(a) rejection based on Dean (US 5,641,487) in view of Chamberlin & Dean (87 PROC. NATL. ACAD. SCI. 6014 (1990)), Applicants' arguments filed 10/03/2003 (See "Section VI") have been carefully considered. The prior 103(a) rejection based on Dean (US 5,641,487) in view of Chamberlin & Dean (87 PROC. NATL. ACAD. SCI. 6014 (1990)) is withdrawn in light of amendments to the claims and in light of the rejection presented in the current action based on Chamberlin & Dean (87 PROC. NATL. ACAD. SCI. 6014 (1990)) in view of Kinloch et al., 92 PROC. NATL. ACAD. SCI. USA 263 (1995) and Rosiere & Wasserman, 154 DEV. BIOL. 309 (1992). Applicants have argued that the sperm-binding and acrosome reaction inducing activity of the claimed polypeptide is demonstrated in the specification (See Remarks p. 13, lines 14-15, filed 10/03/2003). Applicants also argue that Chamberlin & Dean do not describe the claimed polypeptides (See Remarks p. 16, lines 7-8, filed 10/03/2003). Applicants'

arguments have been carefully considered but are not persuasive. A recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. See *In re Casey*, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 136 USPQ 458, 459 (CCPA 1963). Here, as explained *supra*, Applicants' claimed structural differences (i.e. conservative amino acid substitutions) do not distinguish the claimed invention over the prior art because a person or ordinary skill in the art would have been motivated to combine the peptide of Chamberlin & Dean to the ZP3 mutants of Kinloch et al. to provide a peptide of SEQ ID NO: 2 with conservative amino acid substitutions.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new grounds of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J Venci whose telephone number is 571-272-2879. The examiner can normally be reached on 08:00 - 16:30 (EST). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

David J Venci

Examiner

LONG V. LE
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06/28/04